**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

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| In re patent application of | ) | |
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| KUMAR et al. | ) | Group Art Unit: 1625 |
| | ) | |
| Serial No.: 10/591,657 | ) | Examiner: P. L. Morris |
| | ) | |
| Filed: September 5, 2006 | ) | Atty. Dkt. No.: 124907.0106 |
| | ) | |
| For: INDUSTRIAL PROCESS FOR PREPARATION OF CLOPIDOGREL HYDROGEN SULPHATE | ) | |

## PRE-APPEAL BRIEF REQUEST FOR REVIEW

**Mail Stop AF**
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

In response to the Final Office Action mailed December 17, 2008, and the Advisory Action mailed March 20, 2009, Applicants respectfully request a pre-appeal brief review. A Notice of Appeal, a Petition for a one-month extension of time, and associated fees are submitted herewith. The review is requested for the reasons set forth below:

THE CLAIMS ARE NOT INDEFINITE

Claim 56 stands rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Applicants respectfully traverse the rejection.

The Examiner alleges that the recitation of "Form I" is not a universal identification of the compound. The On March 11, 2009, Applicants filed a Response to Final Office Action.

The arguments presented therein are incorporated herein. Applicants further reply to the Final Office Action and Advisory Action as follows:

> Definiteness of claim language must be analyzed, not in a vacuum, but in light of:
>
> (A) The content of the particular application disclosure;
>
> (B) The teachings of the prior art; and
>
> (C) The claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made.

MPEP 2173.02 (emphasis added).

"Form I crystals of (+)-(S)-clopidogrel hydrogen sulphate" is defined in the specification and is generally accepted and has a clear meaning in the art. The content of the specification makes clear that Form I is the same Form I disclosed in WO 99/65915. On page 4, the present specification discloses that "International patent publication, WO 99/65915 (herein referred as '915 patent), disclosed two polymorph forms of Clopidogrel hydrogen sulfate referred to as Form-I and Form-II." Subsequently, on page 18, the specification states:

> The Form I so obtained was characterized by PXRD, DSC and FTIR without any detectable quantity of Form II or other polymorphic Forms with respect to the standard PXRD pattern of Form I as described in '915 patent.

Thus, the specification clearly refers to the same Form I disclosed in WO 99/65915.

The teaching of the prior art is also clear on the meaning of Form I clopidogrel hydrogen sulfate. WO 99/65915 discloses Form I clopidogrel and its powdered X-ray difractogram (PXRD), which shows characteristic peaks at 9.2, 10.9, 15.2, 17.9, 18.5, 20.6, 23.0, 23.2, 23.4, and 25.5±0.2 degrees 2θ. These peaks are confirmed in U.S. Patent No. 6,767,913 as being characteristic of Form I clopidogrel hydrogen sulfate. *See* column 3, lines 15-18. Further, other

patents also refer to the same crystalline form of clopidogrel hydrogen sulfate as Form I. Examples of these patents include U.S. Patent Nos. 7,074,928; 6,800,759; 7,291,735; 6,429,210; and 6,504,030. U.S. Patent No. 7,291,735 discloses that "Clopidogrel bisulfate Form I and II was first time disclosed in International Publication No. WO 99/65915." Both U.S. Patent Nos. 6,429,210 and 6,504,030 issued from the national stage application of WO 99/65915, and thus refer to the same Form I of clopidogrel hydrogen sulfate. Therefore, the teachings of the prior art clearly shows a definite meaning for Form I clopidogrel hydrogen sulfate, all based on the same crystalline form described in WO 99/65915. Thus, from the description of the present specification and the teachings of the prior art, one of ordinary skill in the art would have been able to determine a definite meaning for Form I clopidogrel hydrogen sulfate.

In the Advisory Action, the Examiner alleges that "Applicants have failed to provide any PXRD pattern, elemental analysis for the alleged form." Applicants respectfully submit that Figures 1 and 8 of the present specification clearly show PXRDs of Form I clopidogrel hydrogen sulfate, which are very similar to that of WO 99/65915.

In the Advisory Action, the Examiner avers that "[a]llegations by counsel do NOT take the place of OBJECTIVE EVIDENCE" (emphasis original). Applicants respectfully submit that Applicants have presented prior art references showing a clear and definite meaning for Form I. Applicants have pointed to the present specification to show a clear and definite meaning for Form I. These prior art references and passages in the specification are not mere "allegations by counsel." They are OBJECTIVE EVIDENCE to show that Form I has a clear and definite meaning in the art. Applicants respectfully submit that the Examiner has not provided any specific evidence to contradict Applicants' assertion of definiteness.

In the Final Office Action, page 3, the Examiner alleges that

> X-ray diffraction patters are not the sole parameter for chemical identification because the same chemical material with identical crystalline form can have drastically different powdered [*sic*] diffraction pattern while the same X-ray diffraction pattern can be drawn to different chemicals.

This bald assertion is not supported by any objective evidence. The example cited by the Examiner (Bernstein, p. 118 vs. p. 272) fails to support her assertion, as pointed out by Applicants in the Response filed March 11, 2009, pages 3-4, which is incorporated herein. The Examiner has not responded to or addressed Applicants' position and analysis of Bernstein in the Advisory Action or elsewhere.

For the reasons noted herein and in the Response filed March 11, 2009, Applicants respectfully request withdrawal of the rejection, because overwhelming evidence leads to the conclusion that Form I clopidogrel hydrogen sulfate has a clear and definite meaning in the art.

Applicants have addressed the only outstanding rejection. All claims are now in condition for appeal.

In the event that there are any questions relating to this Request or to the application in general, it would be appreciated if the Examiner would telephone the undersigned attorney concerning such questions so that the prosecution of this application may be expedited.

Please charge any shortage or credit any overpayment of fees to BLANK ROME LLP, Deposit Account No. 23-2185 (124907.0106). In the event that a petition for an extension of time is required to be submitted herewith and in the event that a separate petition does not accompany this response, Applicants hereby petition under 37 C.F.R. 1.136(a) for an extension of time for as many months as are required to render this submission timely.

Any fees due are authorized above.

Respectfully submitted,

Date: May 14, 2009

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